Frontostriatal Maturation Predicts Cognitive Control Failure to Appetitive Cues in Adolescents

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Abstract

■ Adolescent risk-taking is a public health issue that increases the odds of poor lifetime outcomes. One factor thought to influence adolescents' propensity for risk-taking is an enhanced sensitivity to appetitive cues, relative to an immature capacity to exert sufficient cognitive control. We tested this hypothesis by characterizing interactions among ventral striatal, dorsal striatal, and prefrontal cortical regions with varying appetitive load using fMRI scanning. Child, teen, and adult participants performed a go/no-go task with appetitive (happy faces) and neutral cues (calm faces). Impulse control to neutral cues showed linear improvement with age, whereas teens showed a nonlinear reduction in impulse control to appetitive cues. This performance decrement in teens was paralleled by enhanced activity in the ventral striatum. Prefrontal cortical recruitment correlated with overall accuracy and showed a linear response with age for no-go versus go trials. Connectivity analyses identified a ventral frontostriatal circuit including the inferior frontal gyrus and dorsal striatum during no-go versus go trials. Examining recruitment developmentally showed that teens had greater between-subject ventral-dorsal striatal coactivation relative to children and adults for happy no-go versus go trials. These findings implicate exaggerated ventral striatal representation of appetitive cues in adolescents relative to an intermediary cognitive control response. Connectivity and coactivity data suggest these systems communicate at the level of the dorsal striatum differentially across development. Biased responding in this system is one possible mechanism underlying heightened risk-taking during adolescence. ■

INTRODUCTION

Adolescent behavior is qualitatively different from that seen in children and adults in numerous ways. These differences are particularly evident when considering the U.S. health statistics on the prevalence and causes of mortality in teenagers and the heightened risk-taking behavior related to these outcomes. Epidemiological studies report enhanced risk-taking behavior during the adolescent years, as evidenced by substantial influx in drug and alcohol experimentation, accidental death, and unprotected sex (Eaton et al., 2008). A better understanding of the cognitive and biological mechanisms that underlie this behavioral shift may improve targeted interventions aimed to prevent these risky behaviors.

We have developed a theoretical framework characterizing aspects of neurobiological maturation that may bias adolescent behavior toward the approach of expected rewards (Somerville & Casey, 2010; Casey, Getz, & Galvan, 2008; Casey, Jones, & Hare, 2008). This model, consistent with others (Steinberg, 2008; Ernst, Pine, & Hardin, 2006) and grounded in empirical work in the animal and human, proposes that interactions between brain circuitry representing motivational load and cognitive control vary dynamically across development, with adolescence characterized by an imbalance between the relative influence of motivational and control systems on behavior. Specifically, dopamine-rich brain regions representing the appetitive value of potential rewards such as the ventral striatum (Haber & Knutson, 2009; Spicer et al., 2007; Galvan et al., 2005; Wise, 2004; Carlezon & Wise, 1996; Pontieri, Tanda, Orzi, & Di Chiara, 1996) show strong signaling during adolescence, which may be indicative of earlier maturation (Geier, Terwilliger, Teslovich, Velanova, & Luna, 2010; Van Leijenhorst et al., 2009; Galvan et al., 2006). In contrast, brain circuitry important for integrating motivational and cognitive control processes, including ventrolateral frontostriatal networks (Balleine, Delgado, & Hikosaka, 2007; Rubia et al., 2006; Delgado, Stenger, & Fiez, 2004), remain less structurally and functionally mature during the adolescent years (Luna et al., 2001; Giedd et al., 1999). When these systems interact, signaling of the ventral striatum with less down-regulation by control systems exerts a stronger influence on subsequent behavior, effectively signaling enhanced approach motivation left unchecked by control systems.

Although recent neurobiological research has largely supported this conceptualization, the majority of evidence informing these theoretical models has separately targeted either reward processing or cognitive control systems. A notable exception is recent work demonstrating how

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incentive can up-regulate cognitive control abilities (Geier et al., 2010; Hardin et al., 2009), in which participants were rewarded for correctly suppressing an otherwise neutral behavior. Here we address the capacity of adolescents to regulate the approach to appetitive cues themselves by requiring participants to withhold a prepotent response toward faces that are neutral or positive. This design is arguably a relevant experimental model with which to inform adolescents' reduced ability to resist temptation in everyday life.

In the present study, we used a go/no-go paradigm (e.g., Hare, Tottenham, Davidson, Glover, & Casey, 2005; Durston, Davidson, et al., 2003) with happy faces representing appetitive cues and nonthreatening calm faces representing a control condition of lower appetitive value. The assertion that happy faces represent an appetitive stimulus is based on data showing that response latencies to approach happy stimuli (via button press) are speeded relative to less emotional calm expressions (Hare et al., 2005, see Results). This paradigm contains trials in which the participant is instructed to respond to a stimulus and others in which the participant should suppress this response. Child, teen, and adult participants from a sample partially overlapping with a prior report (Hare et al., 2008) completed the task during fMRI scanning. Behavioral responses to each stimulus type were identified, and fMRI analyses focused on circuitry previously implicated in cognitive control across development (frontostriatal circuitry) and areas of the brain sensitive to reward (ventral striatum). Specifically, we focused on how interactions between these systems related to cognitive control failures to salient, appetitive cues across a broad range of ages, including during the transition into and out of adolescence.

METHODS

Participants

Eighty-three participants between the ages of 6 and 29 years were scanned for this experiment. Data from seven participants were excluded for insufficient correct trials to analyze in one or more conditions (not completing all runs of the experiment, poor overall accuracy, and/or lack of responding). Data from 12 participants were excluded on the basis of excessive head motion (as defined by >2 mm translational or 2° rotational motion within a run). Two additional participants were excluded because of technical problems, leaving a total of 62 usable subjects (30 female subjects) in all reported analyses. Portions of the data acquired in this task have been published in a separate report (Hare et al., 2008) focused on an experimental condition not reported on here (see Experimental Task). Relative to the Hare et al. (2008) sample, the present sample consists of $n = 57$ of the same participants and also includes $n = 5$ additional child participants.

For demographic information about the developmental sample, see Table 1. Participants reported no neurological or psychiatric illnesses and no use of psychotropic medications in a brief screening module assessing scanning risks, self-reported health problems, medication usage, and past diagnoses and treatment of psychiatric illnesses. Before participation, all subjects provided informed written consent (parental consent and subject assent for children and adolescents) approved by the institutional review board of Weill Cornell Medical College.

Table 1. Age and Sex Demographics by Age Group

	N	*Age Range*	*Mean Age (SD)*	*% Female*
Children	18	6–12	9.5 (1.64)	50
Teens	19	13–17	15.9 (1.4)	42
Adults	25	18–29	23.7 (3.18)	56

Experimental Task

Participants completed a go/no-go task (Hare et al., 2005, 2008) with fearful, happy, and calm facial expressions serving as stimuli. The current report focuses on the happy and the calm conditions and omits the fear condition from group analyses, which was the focus of a prior report (Hare et al., 2008). Within a single fMRI run, two expression types were presented, one as a go (i.e., target) stimulus to which participants were instructed to press a button and the other expression serving as a no-go (i.e., nontarget) stimulus for which participants should withhold a button press. All combinations of expressions were used as both targets and nontargets resulting in a 2 (Response: go, no-go) × 3 (Emotion: fear, calm, happy) factorial design. Before the onset of each run, a screen appeared indicating which expression served as the target stimulus, instructing participants to respond to that expression and no other expression. Participants were also instructed to respond as fast as possible but to try to avoid making errors.

Stimuli and Apparatus

Stimuli consisted of happy, fearful, and calm faces of unique identities from the NimStim set of facial expressions (Tottenham et al., 2009). Calm faces (mildly pleasant versions of neutral faces) were used because prior work has indicated that neutral faces can be construed as negative in developmental populations (Herba & Phillips, 2004; Thomas et al., 2001; Gross & Ballif, 1991). The task was presented using EPrime software, viewable by subjects on an overhead liquid crystal display panel integrated with the IFIS-SA system (fMRI Devices Corporation, Waukesha, WI). EPrime software, integrated with the IFIS system, logged button responses and RTs.

Task Parameters

Data were acquired in six functional runs representing each combination of emotion (happy, calm, and fear) and

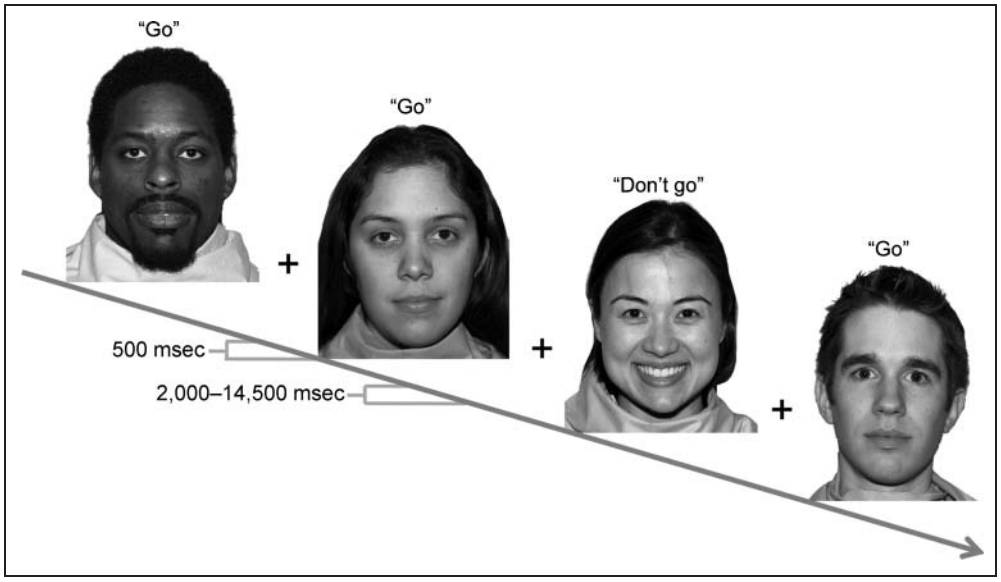

Figure 1. Schematic of four trials within an fMRI run. In this example, calm faces are the target stimuli, for which participants should go by pressing a button. Happy faces are the nontarget (no-go) stimulus, to which participants should withhold a button press. Each face was displayed for 500 msec followed by a variable intertrial interval. Words in quotes above faces were not displayed during the experiment.

response (go and no-go) (Figure 1) using a rapid event-related design. For each trial, a face appeared for 500 msec followed by a jittered intertrial interval ranging from 2 to 14.5 sec in duration (mean 5.2 sec) during which participants rested while viewing a fixation crosshair. A total of 48 trials were presented per run in pseudorandomized order (36 go and 12 no-go). In total, 24 no-go trials and 72 go trials were acquired for each expression type.

Image Acquisition

Participants were scanned with a General Electric Signa 3.0-T fMRI scanner (General Electric Medical Systems, Milwaukee, WI) with a quadrature head coil. A high-resolution, T1-weighted anatomical scan spoiled gradient sequence (256 × 256 in-plane resolution, 240-mm field of view [FOV], 124 × 1.5-mm axial slices) or a 3-D magnetization prepared rapid acquisition gradient-echo sequence (256 × 256 in-plane resolution, 240-mm FOV, 124 × 1.5-mm sagittal slices) was acquired for each subject for transformation and localization of data to Talairach grid space. A spiral in and out sequence (Glover & Thomason, 2004) was used to acquire functional data (repetition time = 2500 msec, echo time = 30 msec, FOV = 200 mm, flip angle = 90, skip 0, 64 × 64 matrix). Thirty-four 4-mm-thick coronal slices were acquired per repetition time a resolution of 3.125 × 3.125 mm covering the entire brain except for the posterior portion of the occipital lobe.

Analysis of Behavioral Data

Behavioral data were analyzed for accuracy by calculating hit (correct response), miss (incorrect lack of response), correct rejection (correct withholding of response), and false alarm (incorrect response) rates for happy and calm conditions. For analysis purposes, participants were grouped into child (aged 6–12 years), teen (aged 13–17 years), and adult (18 years or older) subgroups.

Analysis of fMRI Data

fMRI data analysis was performed within the Analysis of Functional Neuroimages software (AFNI; Cox, 1996). Functional data were slice-time corrected, realigned within and across runs to correct for head movement, coregistered with each participant's high-resolution anatomical scan, scaled to percent signal change units, and smoothed with a 6-mm FWHM Gaussian kernel.

For each participant, a general linear model analysis was performed to characterize task effects by incorporating task regressors of interest (calm–go, calm–no-go, happy–go, happy–no-go, fear–go, fear–no-go, errors) convolved with a gamma-variate hemodynamic response function and covariates of noninterest (motion parameters, linear and quadratic trend for each run). For completeness, fear trials were modeled as task regressors but were not analyzed further. Parameter estimate (β) maps representing task effects were then transformed into the standard coordinate space of Talairach and Tournoux (1988) by applying the warping parameters obtained from the transformation of each subject's high-resolution anatomical scan. Talairach transformed parameter estimate maps were resampled to a resolution of 3 × 3 × 3 mm.

Random effects group analyses were performed to identify functional ROIs for subsequent examination. Specifically, the conditions happy–go, happy–no-go, calm–go, and calm–no-go were carried to a 2 × 2 × 3 group linear mixed effects model with factors of emotion (within-subject: happy and calm), response (within-subject: go and no-go), and age (between-subject: child, teen, and adult). The main effect of response map identified candidate regions differentially engaged as a function of cognitive control demands including the right inferior frontal gyrus (IFG;

$x = 32, y = 23, z = 3$). Responses modulated by development were identified in the main effect of age map, including a cluster in the ventral striatum ($x = -4, y = 11, z = -9$).

Imaging findings considered statistically significant exceeded whole-brain correction for multiple comparisons to preserve an alpha $< .05$ by using a p value/cluster size combination stipulated by Monte Carlo simulations run in the Alphasim program within AFNI. The single exception to whole-brain thresholding was in the analysis of age effects. Given the role of the striatum in the development of impulse control (Somerville & Casey, 2010; Galvan et al., 2006; Durston, Thomas, Yang, et al., 2002; Luna et al., 2001; Casey et al., 2000; Vaidya et al., 1998), it was treated as an *a priori* ROI for voxelwise analysis of age effects. Specifically, age effects were queried for within an inclusive anatomical mask containing voxels in the dorsal and ventral striatum, with $p < .05$, corrected statistical thresholding applied on the basis of the striatum search volume (1,060 voxels). For clarity, we refer to thresholding of the age effect data as $p < .05$, small volume corrected, throughout the manuscript.

ROIs were created as spheres with a 4-mm radius centered about the peaks listed earlier, each containing ten $3 \times 3 \times 3$ voxels. Parameter estimates were extracted for the four conditions (happy–go, happy–no-go, calm–go, and calm–no-go) for each participant and ROI and were submitted to off-line analyses to determine the directionality of effects. Response, emotion, and developmental effects (independent of the voxelwise contrast with which the ROI was defined) were evaluated using 2 (Emotion: calm, happy) $\times$ 2 (Task: go, no-go) $\times$ 3 (Age: child, teen, adult) ANOVAs. Off-line analyses were conducted in SPSS Statistics 17.0 software (SPSS, Chicago, IL).

Significant effects were tested for performance modulation by submitting parameter estimates to bivariate correlations against subjects' mean false alarm rates. Significant performance effects were followed up with partial correlation analyses to test whether performance effects remained significant when controlling for age. Conversely, significant age effects were followed up with partial correlation analyses to identify whether age effects remained significant when controlling for performance.

Prior work with the go–no-go paradigm has established a role for frontostriatal circuitry in supporting successful behavioral inhibition (Hare et al., 2005; Durston, Thomas, Yang, et al., 2002; Casey et al., 2000). To identify this circuitry in the current data set, a psychophysiological interaction (PPI) analysis was used that was sensitive to differential task-based functional connectivity with a seed region in the right IFG, for which regional activity predicted performance differences across ages. Specifically, this analysis was sensitive to brain regions showing greater functional coupling with the right IFG for correct no-go trials relative to go trials. The PPI analysis was carried out using standard processing steps (Friston et al., 1997) by extracting the functional time course within the seed region (right IFG ROI described earlier $x = 32, y = 23, z = 3$), removing sources of noise and artifact, deconvolving the neural signal, and convolving the time-course data with no go versus go task timings and the canonical hemodynamic response function (as specified in Gitelman, Penny, Ashburner, & Friston, 2003). Group results including all participants, thresholded at $p < .05$, corrected for multiple comparisons at the whole-brain level, identified a single cluster showing significantly greater functional connectivity with the right IFG during no-go than to go trials. This cluster extended medial and posterior from the right IFG to the dorsal striatum, specifically to the caudate. A dorsal striatum ROI was generated on the basis of the connectivity map by centering a 4-mm sphere about the cluster subpeak within the anatomical boundaries of the dorsal striatum ($x = 9, y = 13, z = 6$).

Signal change values were extracted from this ROI and tested for between-subject coactivation with the ventral striatum and right IFG. Specifically, ventral striatal, dorsal striatal, and right IFG signal change values from the ROIs previously described were extracted for the happy–no-go versus happy–go contrast. These values were then submitted to between-subject bivariate correlations within child, teen, and adult participant groups. These analyses identify the degree of coactivation across subjects for no-go relative to go trials between these regions within each age group. Identified coactivation values represent the extent to which the tendency to activate one region predicts activation in another region across participants.

Control Analyses

Additional analyses were conducted to verify that reported developmental effects were not due to lower level aspects of the data. As task performance was significantly different across age groups, the number of correct trials varied during first-level general linear model analyses. Therefore, a second set of first-level general linear models was estimated in which the number of correct trials was equated across conditions (happy–go, happy–no-go, calm–go, and calm–no-go) and participants to match the lowest mean number of correct trials across all age groups (calm no-go trials in children; mean = 17). To do so, new regressors were generated by randomly selecting $n = 17$ trials per condition for inclusion. All other trials were modeled but as separate regressors that were not examined further. Findings from the 17-trial regressors were extracted from previously defined ROIs, tested for replication, and reported in Results.

In addition, overall data quality was evaluated across age groups by calculating mean signal-to-noise ratio (SNR) in each of the ventral striatum, dorsal striatum, and right IFG ROIs and in the whole brain. SNR values were computed as the ratio between the mean baseline estimate from first-level general linear modeling and the standard deviation of the residual time series, as described by Murphy, Bodurka, and Bandettini (2007) and used in our previous neuroimaging work (Johnstone et al., 2005). SNR values did not systematically differ across age groups in any of these

regions or in the whole brain (one-way ANOVA [Age: child, teen, adult], ROIs all p values $> .2$; whole brain $p > .3$). Whole-brain SNR values were also included as covariates in the coactivation analyses to verify that between-subject differences could not simply be attributed to differences in data sensitivity within each age group (see Results).

RESULTS

Behavioral Performance

Here we focus on the two types of possible errors in this task: misses (failure to press during go trial) and false alarms (erroneously pressing during no-go trial). For miss rates, results of a 2 (Emotion: happy, calm) × 3 (Age: child, teen, adult) mixed ANOVA yielded a main effect of emotion, $F(1, 59) = 15.44$, $p < .001$, with greater overall miss rates for calm (5.0% ± 0.6%) relative to happy faces (2.6% ± 0.4%). However, tests for a main effect of age, $F(2, 59) = .24$, $p > .7$, and an Age × Emotion interaction, $F(2, 59) = .13$, $p > .8$, were not significant, suggesting that miss rates were not differentially modulated by age for either emotion condition (Figure 2, gray line plots hit rates [inverse of miss rates]). This was further supported by nonsignificant results in independent samples t tests evaluating differential miss rates for happy relative to calm trials in children versus teens, teens versus adults, and children versus adults (all p values $> .5$).

For false alarm rates, we observed a main effect of age, $F(2, 59) = 12.57$, $p < .001$, and an Age × Emotion interaction, $F(2, 59) = 3.59$, $p = .034$ (children: calm, 28.85% ± 4.4%; happy, 26.71% ± 4.2%; teens: calm 22.1% ± 3.4%; happy, 28.4% ± 4.3%; adults: calm, 9.3% ± 1.5%; happy, 8.9% ± 1.7%) and no main effect of emotion, $F(1, 59) = 1.18$, $p > .2$ (Figure 2, black line). To explore the directionality of the interaction, we conducted a series of independent samples t tests comparing false alarm rates for happy relative to calm trials across age groups. Teens generated significantly more false alarms for happy relative to calm trials compared with children, $t(35) = 2.04$, $p = .049$, and adults, $t(42) = 2.62$, $p = .012$. Demonstrated another way, the false alarms committed by adolescents were significantly loaded in the happy condition (happy versus calm), $t(18) = 2.87$, $p = .01$, whereas the false alarms committed by children and adults were equally distributed across happy and calm expression types (happy versus calm; children $p > .5$, adults $p > .9$). Finally, for calm trials, false alarms demonstrated a linear pattern of improvement with increasing age, linear term, $F(1, 59) = 22.3$, $p < .001$, quadratic term $p > .4$, whereas for the happy trials, quadratic (inverted U) and linear contrasts explained a significant portion of the variance in responding, quadratic term, $F(1, 59) = 6.52$, $p = .013$, linear $F(1, 59) = 14.31$, $p < .001$.

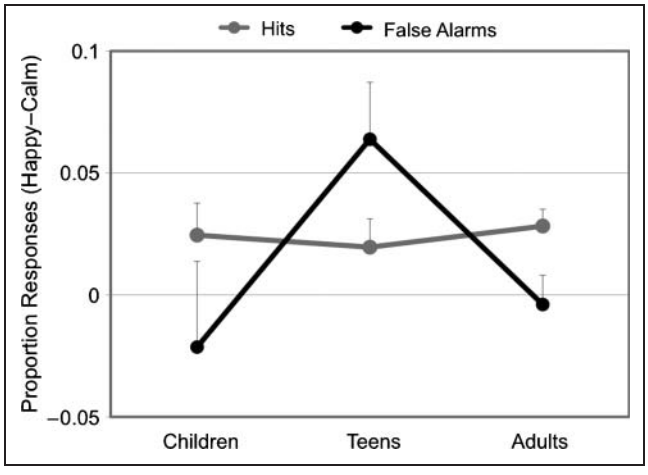

Figure 2. Behavioral performance by emotion and development. Gray line represents proportion of correct hits out of total go trials; black line represents proportion of false alarms out of total no-go trials. The y-axis represents the proportion of responses for happy trials adjusted for proportion of responses for calm trials.

RT data suggest that happy faces facilitate speeded responses relative to calm faces (mean speeding to happy relative to calm ± SD = 53.5 ± 68 msec), $F(1, 59) = 36.09$, $p < .001$. This effect was evident in all three age groups when tested separately (p values ≤ .01). Descriptive RT data are as follows: children (mean RT ± SD, in milliseconds: calm = 767.7 ± 194; happy = 710.0 ± 186), teens (calm = 549 ± 91; happy = 518.9 ± 86), and adults (calm = 626.4 ± 100; happy = 558.0 ± 66).

To test whether differential error rates across age groups could be explained by a general speed-accuracy tradeoff, we analyzed RT data for correct go trials. A speed-accuracy tradeoff account could explain the differential accuracy findings across age if the conditions of poorest accuracy were also the fastest. We found no evidence of speed-accuracy tradeoff effects because unlike the accuracy findings, the test for an interaction between age and emotion in RTs was not significant, $F(2, 59) = 1.78$, $p > .15$. In other words, all three groups demonstrated equivalently speeded responses to happy faces that did not mirror the accuracy findings.

fMRI Results

Responses modulated by development were identified in the main effect of age map, including a cluster in the ventral striatum ($x = -4$, $y = 11$, $z = -9$; $p < .05$, small volume corrected; Figure 3A). Post hoc analysis of the age main effect showed that adolescents engaged the ventral striatum significantly compared with children and adults to happy faces (p values ≤ .01; Figure 3B) and to a lesser extent to calm faces (p values ≤ .06; means ± SD of percent signal change for calm versus rest: children = −0.095 ± 0.21; teens = 0.046 ± 0.16; adults = −0.051 ± 0.17). Analysis of the best-fitting function that represents responding across ages to happy faces showed that a quadratic (inverted U) function explained a significant portion of variance in the ventral striatal response to happy faces, $F(1, 59) = 10.05$, $p < .003$, whereas a linear function did

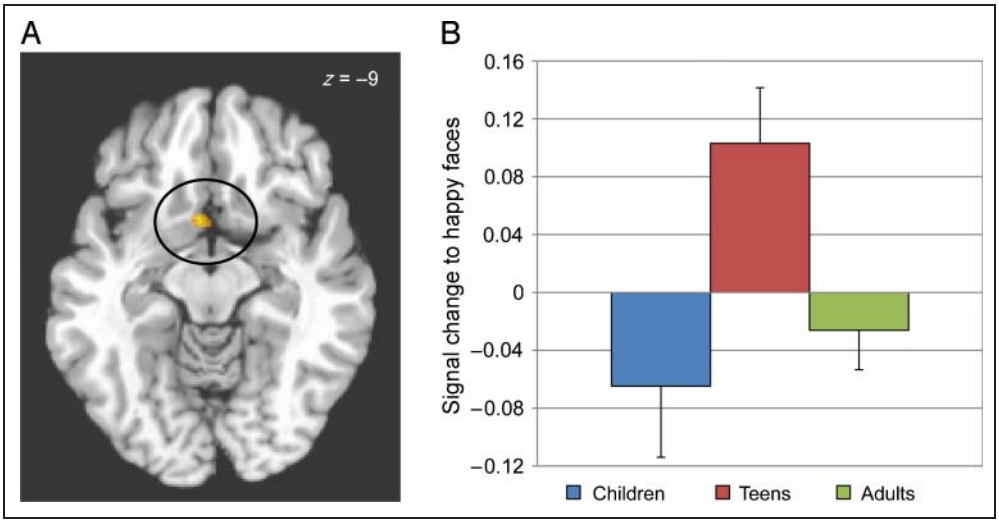

Figure 3. (A) Brain regions showing differential activity as a function of age. Activations, threshold $p < .05$, small volume corrected, are rendered on a representative high-resolution anatomical scan. (B) Plot of activity in the ventral striatum (circled in panel A) response to happy faces (no-go and go conditions collapsed) relative to rest as a function of age. Adolescents show a significantly larger magnitude of activation relative to both children and adults. The left side of image corresponds to the left side of the brain.

not, $F(1, 59) = 0.54$, $p > .4$. The nonlinear enhancement in recruitment in teens remained significant when controlling for differences in task performance (false alarm rate; $F(2, 59) = 6.77$, $p < .002$) and in the control analysis with matched numbers of trials, $F(2, 59) = 7.80$, $p = .007$. The magnitude of activity to happy trials, calm trials, and no-go versus go trials was not associated with task performance (p values $> .2$).

The main effect of response map (no-go versus go) identified regions differentially engaged as a function of cognitive control demands including the right IFG ($x = 32, y = 23, z = 3$), showing significantly greater responses to no-go relative to go trials (p values $< .05$, whole-brain corrected; Figure 4A). Post hoc analyses testing for the best fitting function indicated the right IFG response was significantly explained by a linear function, $F(1, 59) = 4.53$, $p = .037$, and not a quadratic function, $F(1, 59) = .17$, $p > .6$. Post hoc analyses indicated that the right IFG also showed greater activity to calm relative to happy faces, $F(2, 59) = 8.95$, $p < .005$. Further, the right IFG ROI showed a linear decrease in response magnitude with increasing age to no-go trials relative to go trials, $r(61) = -0.28$, $p = .026$ (Figure 4B).

When controlling for performance effects, the Task × Age interaction in the right IFG was no longer significant ($p > .4$), indicating performance was a more robust predictor of activity in the right IFG than age. This relationship was demonstrated by a significant correlation between response magnitude to correct no-go versus go trials and overall performance (as measured by false alarm rate),

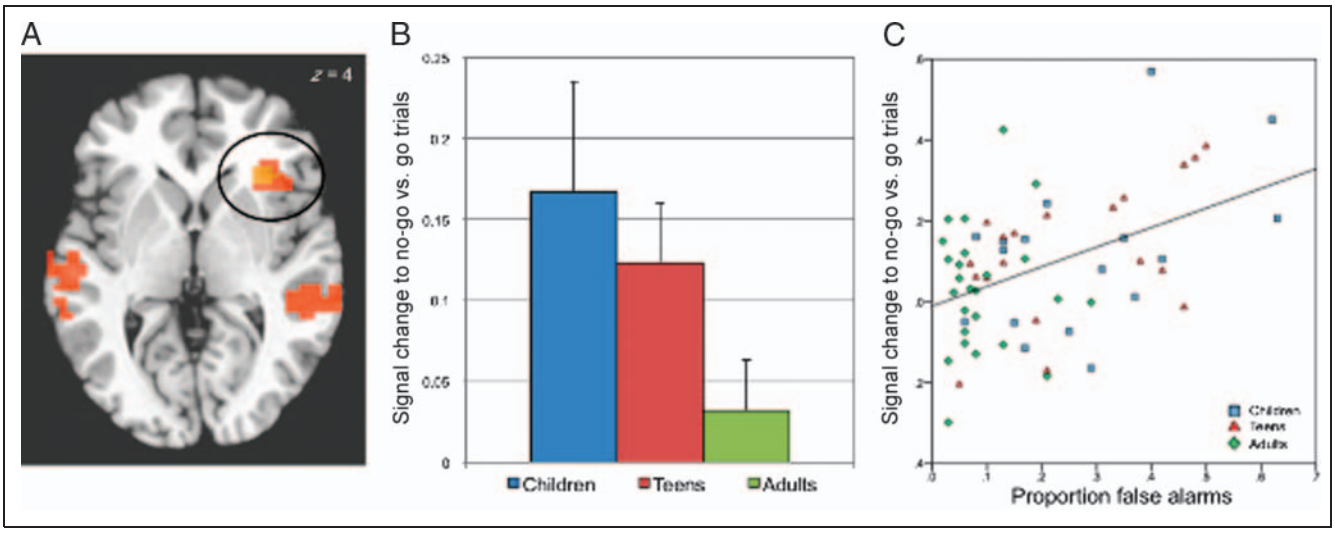

Figure 4. (A) Brain regions showing differential activity as a function of task (no-go > go). Activations, thresholded $p < .05$, whole-brain corrected, are rendered on a representative high-resolution anatomical scan. (B) Plot of activity in the right IFG (circled in A) to no-go relative to go trials (happy and calm conditions collapsed) as a function of age. Increasing age predicts a linear decrease in recruitment. (C) Plot of activity in panel A as a function of performance. Generally, worse performance (greater false alarm rate on x-axis) predicted greater recruitment for successful suppression trials (correct no-go trials collapsed across emotion) relative to go trials (collapsed across emotion). The left side of image corresponds to the left side of the brain.

$r(61) = 0.39, p = .002$ (see Figure 4C), which was replicated in the control analysis with a matched number of trials, $r(61) = 0.28, p = .026$. Figure 4C depicts this relationship with one participant excluded who was found to be an extreme outlier (defined as more than three interquartile ranges above the third or below the first quartile value). Although the correlation is significant including this individual, excluding this individual renders the resulting correlation even more reliable, $r(60) = 0.45, p < .001$. All reported analyses represent responses to correct trials. Thus, individuals more susceptible to false alarms tend to recruit the right IFG more to the no-go trials for which they successfully suppressed a behavioral response.

Connectivity Analyses

The PPI analysis yielded a single cluster of voxels showing significantly greater functional connectivity with the right IFG for correct no-go trials relative to go trials. This cluster extends from near the right IFG seed region medially and posteriorly into the right dorsal striatum ($x = 9, y = 13, z = 6$; see Figure 5). These findings implicate a functional frontostriatal circuit showing significantly greater coordinated activity during trials in which response suppression was correctly engaged relative to trials in which response suppression was not required.

Follow-up analyses tested whether frontostriatal circuitry showed differential degrees of coactivity across ages for no-go relative to go trials. A series of between-subject correlations tested the degree of coactivation between ROI signal values (no-go vs. go contrast) from the ventral striatum (shown in Figure 3), the right IFG (shown in Figure 4), and the dorsal striatum (shown in Figure 5) within each age group. Data for the happy condition are summarized in Figure 6. We focus on the happy condition because happy–no-go relative to happy–go trials encompass the psychological construct of suppressing approach responses toward appetitive cues. Children showed marginal coactivation between the ventral striatum and the dorsal striatum during happy no-go versus go trials, $r(17) = 0.41$, $p = .09$, whereas coactivation between the dorsal striatum and the right IFG was less reliable ($p > .12$). Conversely, adults showed significant coactivation between the dorsal striatum and the right IFG, $r(24) = 0.49, p = .013$, but not between the ventral striatum and the dorsal striatum ($p > .8$). Teens showed significant coactivation between the ventral and the dorsal striata, $r(18) = 0.57, p = .012$, as well as the dorsal striatum and right IFG, $r(18) = 0.54$, $p = .016$. All correlations remained significant in partial correlation analyses controlling for differences in whole-brain signal to noise ratio across participants with the exception of the dorsal striatum-right IFG correlation in adults, which becomes a nonsignificant positive trend.

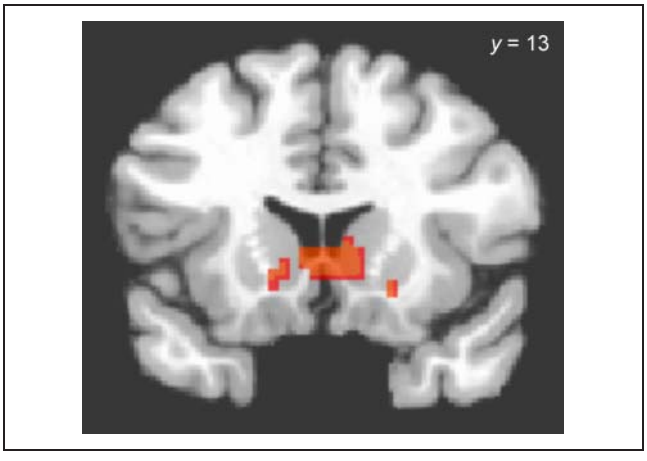

Figure 5. PPI results based on seed region in right IFG (circled in Figure 4A). The right dorsal striatum (caudate) demonstrates significantly greater functional coupling with the right IFG during no-go relative to go trials (threshold $p < .05$, whole-brain corrected and rendered on a representative high-resolution anatomical scan). The left side of image corresponds to the left side of the brain.

DISCUSSION

The capacity to exert control over one's actions is especially challenged when confronted with salient, appetitive cues. In this study, we sought to provide empirical evidence for reduced impulse control in adolescents when faced with cues signaling appetitive value. Using a task that contains salient, appetitive stimuli (e.g., happy faces) that facilitated approach responses, we tested the developmental trajectory of subjects' ability to flexibly approach or avoid positive or neutral stimuli in a context-dependent manner. We found that teens demonstrated a unique pattern of errors relative to both children and adults, characterized by a reduction in the capacity to suppress approach behavior toward a salient, appetitive cue.

These behavioral findings suggest that although adolescents can engage behavioral suppression in neutral contexts at a proficiency intermediate to children and adults, they demonstrate a specific failure to override approach motivation toward appetitive cues. These findings cannot simply be explained by speed-accuracy tradeoff effects because each of the three age groups demonstrated faster performance to happy than neutral cues, which did not predict poorer performance. This behavioral profile is consistent with theoretical accounts of adolescents as biased to engage in risky behavior at the service of approaching potential rewards (Steinberg, 2004) and converges with animal models of development showing enhanced reward seeking during developmental periods comparable with adolescence (Spear, 2000). Recently, Cauffman et al. (2010) used a series of decision making tasks with varying reward load and demonstrated that reward sensitivity shows an inverse U-shaped function, rising to peak from 14 to 16 years of age and then declining. Laboratory demonstrations of biased approach motivation in adolescents (see also Figner, Mackinlay, Wilkening, & Weber, 2009) bolster

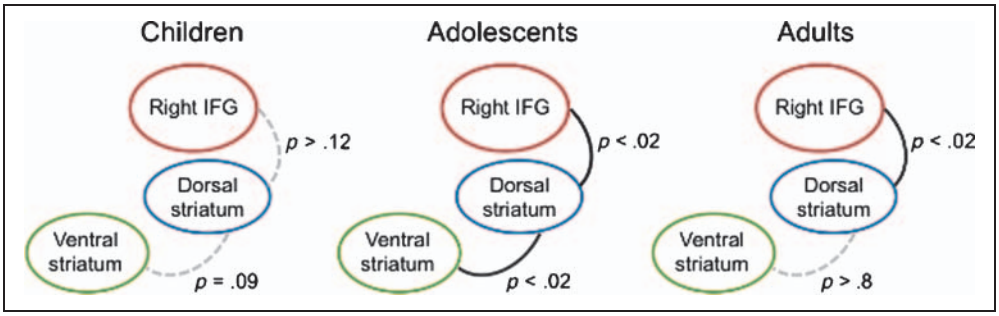

Figure 6. Between-subject functional coactivation results for happy no-go trials relative to happy go trials in child, adolescent, and adult participants. Labeled bubbles represent regions depicted in Figure 3 (ventral striatum), Figure 4 (right IFG), and Figure 5 (dorsal striatum). *p* values represent level of coactivation across participants. Dotted line: coactivation not significant; gray line: significant at $p < .05$. All correlations are positive. IFG = inferior frontal gyrus.

the conclusion that adolescent risk-taking behavior is not simply a function of changes in independence or societal treatment (e.g., Epstein, 2007; for further discussion, see Dahl, 2004). It is also not solely attributable to immature cognitive regulation abilities (Yurgelun-Todd, 2007), as motivational aspects of the environment influence the ability to regulate behavior in a given context. Rather, this work suggests that the maturation trajectories of both cognitive and affective processes interact to influence the influx in risk taking during adolescence (Casey, Getz, et al., 2008; Steinberg, 2008). The current behavioral findings suggest that when required to suppress behavioral approach to salient appetitive cues, adolescents' performance shows impairment not observed in other age groups.

Behavioral findings lead to neurobiological hypotheses regarding differential maturation of cognitive control and motivational systems. On the basis of nonhuman and human work to date, we specifically targeted frontostriatal and ventral striatal circuitry as candidate regions whose dynamic interactions across development are thought to mediate adolescents' reduced ability to resist approaching potential rewards (Somerville & Casey, 2010). We observed a region of the ventral striatum showing a nonlinear pattern of engagement with maximal activity in teens to happy faces. This finding converges with prior work demonstrating exaggerated representation of reward properties of stimuli in adolescents. For example, receipt of a monetary incentive led to exaggerated responses in the ventral striatum of adolescents compared with adults (Ernst et al., 2005) and children (Van Leijenhorst et al., 2009; Galvan et al., 2006). Relative to adults, adolescents show enhanced ventral striatal activity while preparing for a trial for which reward is at stake (Geier et al., 2010), suggesting up-regulation of motivated behavior at the level of ventral striatum in adolescents. In addition, we observed a marginally greater response to neutral facial expressions in adolescents in the ventral striatum, although to a lesser extent than happy faces. This pattern suggests that although appetitive stimuli recruit ventral striatal responses more prominently, engagement of the ventral striatum in adolescents may also be marked by reduced specificity relative to children and adults.

Comparing no-go with go trials enabled the isolation of responses to trials in which suppression was correctly engaged (no-go trials) relative to trials in which cognitive control demands were low. It should be noted that as in past work (Hare et al., 2005, 2008; Durston, Davidson, et al., 2003), error trials were modeled separately, and thus activity differences here represent those to which correct suppression was accomplished. During no-go trials, we observed greater prefrontal recruitment in individuals with younger age. Prefrontal activity also predicted performance, such that individuals who were overall less successful at suppressing approach responses showed more right IFG activity for successful suppression trials. This pattern is consistent with prior work using the go/no-go paradigm (Luna & Sweeney, 2004; Durston, Davidson, et al., 2003; Durston, Thomas, Yang, et al., 2002), reporting engagement of the IFG for trials in which suppression was correctly invoked. The relationship between activity and performance suggests that prefrontal control resources were engaged to a greater degree in individuals who had the most difficulty accomplishing response suppression (i.e., younger participants).

More generally, there is less agreement in the literature about the nature of developmental shifts in recruitment of lateral prefrontal regions in contexts of cognitive demand. In the current study, we relied on differences in behavioral performance to interpret age-related changes in activation magnitude. Some studies, consistent with what is presented here, have demonstrated progressively lesser recruitment of prefrontal cortical regions with increasing age (Hardin et al., 2009; Velanova, Wheeler, & Luna, 2008). This pattern could be interpreted as a relatively less specialization in younger populations resulting in more diffuse engagement (Durston et al., 2006). Greater recruitment in younger ages may also be a result of increasing cognitive demands required of younger individuals to successfully complete the same task as older individuals, as suggested by Velanova et al. (2008) on the basis of similar findings using an antisaccade task. Using performance variability, our observation that greater recruitment was found in the participants who had the greatest number of false alarm errors

supports this interpretation. However, it should be noted that there is still debate as to whether stronger or weaker activation is a marker of "maturity" (Luna, Padmanabhan, & O'Hearn, 2010; Bunge & Wright, 2007) as other work has suggested larger magnitude activity as an indicator of functional maturation (Crone, Wendelken, Donohue, van Leijenhorst, & Bunge, 2006; Rubia et al., 2006; Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002; Klingberg, Forssberg, & Westerberg, 2002). Future developmental work will be required to more fully inform this issue.

Connectivity analyses identified frontostriatal circuitry, specifically the right dorsal caudate and IFG that demonstrated significantly stronger functional coupling during correct suppression trials relative to trials not requiring suppression. Striatocortical interactions have been shown across tasks and species to be central to accomplishing goal-directed behavioral regulation (Delgado et al., 2004; Durston, Thomas, Yang, et al., 2002; Schultz, Tremblay, & Hollerman, 2000) and more specifically in the suppression of impulses (Miller & Cohen, 2001). Interactions between the dorsal striatum and the PFC have been shown in primates to be critical to integrating reward associations with behavioral output (Pasupathy & Miller, 2005), a finding paralleled by adult human imaging literature (Galvan et al., 2005; Poldrack, Prabhakaran, Seger, & Gabrieli, 1999). Developmentally, engagement of right frontostriatal circuits supports suppression of a compelling response in children and adults (Durston, Thomas, Worden, Yang, & Casey, 2002; Durston, Thomas, Yang, et al., 2002; Casey et al., 1997) and is hyporesponsive in impulse control disorders such as attention deficit hyperactivity disorder (Casey et al., 2007; Epstein et al., 2007; Durston, Tottenham, et al., 2003; Vaidya et al., 1998). These findings support a general role for this circuitry in the shaping of goal-oriented actions.

After defining this circuitry, we tested for differential coactivation patterns among child, adolescent, and adult participants. Adult and teen participants showed significant between-subject coupling of dorsal striatal-prefrontal responses. In other words, adult and teen participants who tended to engage the dorsal striatum also tended to engage the inferior frontal cortex when correctly suppressing approach responses to happy faces. Although indirect, these findings support the notion that striatocortical responses show a relatively greater degree of functional organization in teens and adults relative to children. In adolescent participants, this frontostriatal response was also accompanied by a significant ventral-dorsal striatal coupling. On the basis of what is known about this circuitry (Haber, Kim, Mailly, & Calzavara, 2006), we speculate that teens who tended to activate the ventral striatum more strongly also required greater dorsal striatal-prefrontal engagement to correctly suppress approach to positive cues.

Interactions between the ventral striatum, the dorsal striatum, and the PFC are critical to the learning, expression, and regulation of motivated behavior. Indeed, individuals with Parkinson's disease who suffer from focal disruption of striatal function demonstrate selective deficits in identifying and selecting motivationally relevant information in the environment (Cools, Ivry, & D'Esposito, 2006). By tracking anatomical projection fields, work by Haber et al. (2006) has implicated the dorsal striatum as a key convergence point for valuation-relevant signaling from the ventral striatum and signals from regions of the brain important for cognitive control, including the PFC (see also Haber & Knutson, 2009). Moreover, "parallel" striatocortical loops involved in different forms of goal-directed behavior (motor, oculomotor, stimulus driven, response driven, or motivational) have long been suggested to communicate at the level of the BG (Casey, Tottenham, & Fossella, 2002; Casey, Durston, & Fossella, 2001; Casey, 2000; Alexander & Crutcher, 1990). Our findings are consistent with differential biasing of these loops at the level of the striatum, when subcortical systems appear to be reaching functional maturity and suggest that while signaling of subcortical regions develops relatively early, top–down signaling from these control regions may be more protracted.

Limitations

The findings presented here should be considered in light of their limitations. First, it should be explicitly acknowledged that a third emotional category, fearful faces, was present during the experimental task and the focus of a previous report (Hare et al., 2008). The calm face condition served as a control condition in both reports. Although behavioral findings suggest the presence of fearful faces in a functional scan did not modulate behavioral accuracy differently than the other two emotion categories, it is possible that the presence of fearful faces influenced the findings in ways to which the available measures were not sensitive. In addition, happy faces differ from calm faces in valence and salience, both of which could have contributed to the observed effects of appetitive value. A second methodological limitation is in the use of calm faces as a control condition. Although normative data suggest that calm faces are less positive and arousing than happy faces (Tottenham et al., 2009), we did not explicitly collect these ratings, and it is possible that the calm faces were interpreted as mildly positive in their own right. In terms of results, the modest nature of the coactivation findings should also be acknowledged. Finally, measures of pubertal status and endogenous hormones were not acquired. Seminal research has demonstrated ways in which circulating gonadal hormones affect both organizational and activational mechanisms to influence brain function across development (Steinberg, 2008; Sisk & Foster, 2004; Romeo & Sisk, 2001) and has shown a predictive relationship between pubertal status and such appetitive behaviors as sensation seeking and drug abuse (Martin et al., 2002; see Forbes & Dahl, 2010). Future research including measures of hormones may inform the relationship between striatocortical development, hormonal maturation, and behavioral outcomes (Blakemore, Burnett, & Dahl, 2010).

Conclusion

Adolescence has been described as a period of social reorientation (Nelson, Leibenluft, McClure, & Pine, 2005), with less time spent with parents and more time spent with peers, relatively unmonitored. With this relative influx in freedom comes an increasing need to regulate one's own behavior, which contrasts with childhood when behavior tends to be constrained by parents and other caregivers. Although immature cognitive control capacity has often been considered a sufficient explanation for adolescents' influx in risky behavior, there is a growing body of evidence including the current findings implicating biased motivational drives in adolescence, both at the behavioral and neurobiological level. Indeed, the relatively greater freedom experienced during this time may support stronger motivational drives, as independence also facilitates opportunity to seek out potentially rewarding experiences. This approach motivation may be supported by strong subcortical signaling of the ventral striatum. When placed in contexts in which one must regulate their own behavior, control failures—some resulting in risky behavior—may be a product of strong motivational drives combined with a prefrontal regulatory system that is relatively inexperienced and thus not functionally mature. Over time, experience shapes the capacity to regulate these approach behaviors, which shifts toward a state of greater balance between dynamic approach and regulatory signaling circuitries and strengthening of the ability to resist temptation.

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REFERENCES

Alexander, G. E., & Crutcher, M. D. (1990). Functional architecture of basal ganglia circuits: Neural substrates of parallel processing. *Trends in Neurosciences, 13,* 266–271.

Balleine, B. W., Delgado, M. R., & Hikosaka, O. (2007). The role of the dorsal striatum in reward and decision-making. *Journal of Neuroscience, 27,* 8161–8165.

Blakemore, S. J., Burnett, S., & Dahl, R. E. (2010). The role of puberty in the developing adolescent brain. *Human Brain Mapping, 31,* 926–933.

Bunge, S. A., Dudukovic, N. M., Thomason, M. E., Vaidya, C. J., & Gabrieli, J. D. (2002). Immature frontal lobe contributions to cognitive control in children: Evidence from fMRI. *Neuron, 33,* 301–311.

Bunge, S. A., & Wright, S. B. (2007). Neurodevelopmental changes in working memory and cognitive control. *Current Opinion in Neurobiology, 17,* 243–250.

Carlezon, W. A., & Wise, R. A. (1996). Rewarding actions of phencyclidine and related drugs in nuleus accumbens shell and orbitofrontal cortex. *Journal of Neuroscience, 16,* 3112–3122.

Casey, B. J. (2000). Disruption of inhibitory control in developmental disorders: A mechanistic model of implicated frontostriatal circuitry. In R. S. Siegler & J. L. McClelland (Eds.), *Mechanisms of cognitive development: The Carnegie symposium on cognition* (Vol. 28, pp. 327–352). Hillsdale, NJ: Erlbaum.

Casey, B. J., Castellanos, F. X., Giedd, J. N., Marsh, W. L., Hamburger, S. D., Schubert, A. B., et al. (1997). Implication of right frontostriatal circuitry in response inhibition and attention-deficit/hyperactivity disorder. *Journal of American Academy of Child and Adolescent Psychiatry, 36,* 374–383.

Casey, B. J., Durston, S., & Fossella, J. A. (2001). Evidence for a maechanistic model of cognitive control. *Clinical Neuroscience Research, 1,* 267–282.

Casey, B. J., Epstein, J. N., Buhle, J., Liston, C., Davidson, M. C., Tonev, S. T., et al. (2007). Frontostriatal connectivity and its role in cognitive control in parent-child dyads with ADHD. *American Journal of Psychiatry, 164,* 1729–1736.

Casey, B. J., Getz, S., & Galvan, A. (2008). The adolescent brain. *Developmental Review, 28,* 62–77.

Casey, B. J., Jones, R. M., & Hare, T. (2008). The adolescent brain. *Annals of the New York Academy of Sciences, 1124,* 111–126.

Casey, B. J., Thomas, K. M., Welsh, T. F., Badgaiyan, R. D., Eccard, C. H., Jennings, J. R., et al. (2000). Dissociation of response conflict, attentional selection, and expectancy with functional magnetic resonance imaging. *Proceedings of the National Academy of Sciences, U.S.A., 97,* 8728–8733.

Casey, B. J., Tottenham, N., & Fossella, J. (2002). Clinical, imaging, lesion, and genetic approaches toward a model of cognitive control. *Developmental Psychobiology, 40,* 237–254.

Cauffman, E., Shulman, E. P., Steinberg, L., Claus, E., Banich, M. T., Graham, S. J., et al. (2010). Age differences in affective decision making as indexed by performance on the Iowa Gambling Task. *Developmental Psychology, 46,* 193–207.

Cools, R., Ivry, R. B., & D'Esposito, M. (2006). The human striatum is necessary for responding to changes in stimulus relevance. *Journal of Cognitive Neuroscience, 18,* 1973–1983.

Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, 29,* 162–173.

Crone, E. A., Wendelken, C., Donohue, S., van Leijenhorst, L., & Bunge, S. A. (2006). Neurocognitive development of the ability to manipulate information in working memory. *Proceedings of the National Academy of Sciences, U.S.A., 103,* 9315–9320.

Dahl, R. E. (2004). Adolescent brain development: A period of vulnerabilities and opportunities. *Annals of the New York Academy of Sciences, 1021,* 1–22.

Delgado, M. R., Stenger, V. A., & Fiez, J. A. (2004). Motivation-dependent responses in the human caudate nucleus. *Cerebral Cortex, 14,* 1022–1030.

Durston, S., Davidson, M. C., Thomas, K. M., Worden, M. S., Tottenham, N., Martinez, A., et al. (2003). Parametric manipulation of conflict and response competition using

rapid mixed-trial event-related fMRI. *Neuroimage, 20,* 2135–2141.
Durston, S., Davidson, M. C., Tottenham, N., Galvan, A., Spicer, J., Fossella, J. A., et al. (2006). A shift from diffuse to focal cortical activity with development. *Developmental Science, 9,* 1–8.
Durston, S., Thomas, K. M., Worden, M. S., Yang, Y., & Casey, B. J. (2002). The effect of preceding context on inhibition: An event-related fMRI study. *Neuroimage, 16,* 449–453.
Durston, S., Thomas, K. M., Yang, Y., Ulug, A. M., Zimmerman, R. D., & Casey, B. J. (2002). A neural basis for the development of inhibitory control. *Developmental Science, 5,* F9–F16.
Durston, S., Tottenham, N. T., Thomas, K. M., Davidson, M. C., Eigsti, I. M., Yang, Y., et al. (2003). Differential patterns of striatal activation in young children with and without ADHD. *Biological Psychiatry, 53,* 871–878.
Eaton, L. K., Kann, L., Kinchen, S., Shanklin, S., Ross, J., Hawkins, J., et al. (2008). Youth Risk Behavior Surveillance—United States, 2007, surveillance summaries. *Morbidity and Mortality Weekly Report, 57,* 1–131.
Epstein, J. N., Casey, B. J., Tonev, S. T., Davidson, M., Reiss, A. L., Garrett, A., et al. (2007). ADHD- and medication-related brain activation effects in concordantly affected parent–child dyads with ADHD. *Journal of Child Psychology and Psychiatry, 48,* 899–913.
Epstein, R. (2007). *The case against adolescence: Rediscovering the adult in every teen*. Fresno, CA: Quill Driver Books.
Ernst, M., Nelson, E. E., Jazbec, S., McClure, E. B., Monk, C. S., Leibenluft, E., et al. (2005). Amygdala and nucleus accumbens in responses to receipt and omission of gains in adults and adolescents. *Neuroimage, 25,* 1279–1291.
Ernst, M., Pine, D. S., & Hardin, M. (2006). Triadic model of the neurobiology of motivated behavior in adolescence. *Psychological Medicine, 36,* 299–312.
Figner, B., Mackinlay, R. J., Wilkening, F., & Weber, E. U. (2009). Affective and deliberative processes in risky choice: Age differences in risk taking in the Columbia Card Task. *Journal of Experimental Psychology: Learning, Memory, and Cognition, 35,* 709–730.
Forbes, E. E., & Dahl, R. E. (2010). Pubertal development and behavior: Hormonal activation of social and motivational tendencies. *Brain and Cognition, 72,* 66–72.
Friston, K. J., Buechel, C., Fink, G. R., Morris, J., Rolls, E., & Dolan, R. J. (1997). Psychophysiological and modulatory interactions in neuroimaging. *Neuroimage, 6,* 218–229.
Galvan, A., Hare, T. A., Davidson, M., Spicer, J., Glover, G., & Casey, B. J. (2005). The role of ventral frontostriatal circuitry in reward-based learning in humans. *Journal of Neuroscience, 25,* 8650–8656.
Galvan, A., Hare, T. A., Parra, C. E., Penn, J., Voss, H., Glover, G., et al. (2006). Earlier development of the accumbens relative to orbitofrontal cortex might underlie risk-taking behavior in adolescents. *Journal of Neuroscience, 26,* 6885–6892.
Geier, C. F., Terwilliger, R., Teslovich, T., Velanova, K., & Luna, B. (2010). Immaturities in reward processing and its influence on inhibitory control in adolescence. *Cerebral Cortex, 20,* 1613–1629.
Giedd, J. N., Blumenthal, J., Jeffries, N. O., Castellanos, F. X., Liu, H., Zijdenbos, A., et al. (1999). Brain development during childhood and adolescence: A longitudinal MRI study. *Nature Neuroscience, 2,* 861–863.
Gitelman, D. R., Penny, W. D., Ashburner, J., & Friston, K. J. (2003). Modeling regional and psychophysiologic interactions in fMRI: The importance of hemodynamic deconvolution. *Neuroimage, 19,* 200–207.
Glover, G. H., & Thomason, M. E. (2004). Improved combination of spiral-in/out images for BOLD fMRI. *Magnetic Resonance in Medicine, 51,* 863–868.
Gross, A. L., & Ballif, B. (1991). Children's understanding of emotion from facial expressions and situations: A review. *Developmental Review, 11,* 368–398.
Haber, S. N., Kim, K. S., Mailly, P., & Calzavara, R. (2006). Reward-related cortical inputs define a large striatal region in primates that interface with associative cortical connections, providing a substrate for incentive-based learning. *Journal of Neuroscience, 26,* 8368–8376.
Haber, S. N., & Knutson, B. (2009). The reward circuity: Linking primate anatomy and human imaging. *Neuropsychopharmacology, 1,* 1–23.
Hardin, M. G., Mandell, D., Mueller, S. C., Dahl, R. E., Pine, D. S., & Ernst, M. (2009). Inhibitory control in anxious and healthy adolescents is modulated by incentive and incidental affective stimuli. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 50,* 1550–1558.
Hare, T. A., Tottenham, N., Davidson, M. C., Glover, G. H., & Casey, B. J. (2005). Contributions of amygdala and striatal activity in emotion regulation. *Biological Psychiatry, 57,* 624–632.
Hare, T. A., Tottenham, N., Galvan, A., Voss, H. U., Glover, G. H., & Casey, B. J. (2008). Biological substrates of emotional reactivity and regulation in adolescence during an emotional go–nogo task. *Biological Psychiatry, 63,* 927–934.
Herba, C., & Phillips, M. (2004). Annotation: Development of facial expression recognition from childhood to adolescence: Behavioral and neurological perspectives. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 45,* 1185–1198.
Johnstone, T., Somerville, L. H., Alexander, A. L., Davidson, R. J., Kalin, N. H., & Whalen, P. J. (2005). Stability of amygdala BOLD response to fearful faces over multiple scan sessions. *Neuroimage, 25,* 1112–1123.
Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Increased brain activity in frontal and parietal cortex underlies the development of visuospatial working memory capacity during childhood. *Journal of Cognitive Neuroscience, 14,* 1–10.
Luna, B., Padmanabhan, A., & O'Hearn, K. (2010). What has fMRI told us about the development of cognitive control through adolescence? *Brain and Cognition, 72,* 101–113.
Luna, B., & Sweeney, J. A. (2004). The emergence of collaborative brain function: fMRI studies of the development of response inhibition. *Annals of the New York Academy of Sciences, 1021,* 296–309.
Luna, B., Thulborn, K. R., Munoz, D. P., Merriam, E. P., Garver, K. E., Minshew, N. J., et al. (2001). Maturation of widely distributed brain function subserves cognitive development. *Neuroimage, 13,* 786–793.
Martin, C. A., Kelly, T. H., Rayens, M. K., Brogli, B. R., Brenzel, A., Smith, W. J., et al. (2002). Sensation seeking, puberty, and nicotine, alcohol, and marijuana use in adolescence. *Journal of American Academy of Child and Adolescent Psychiatry, 41,* 1495–1502.
Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24,* 167–202.
Murphy, K., Bodurka, J., & Bandettini, P. A. (2007). How long to scan? The relationship between fMRI temporal signal to noise ratio and necessary scan duration. *Neuroimage, 34,* 565–574.
Nelson, E. E., Leibenluft, E., McClure, E. B., & Pine, D. S. (2005). The social re-orientation of adolescence: A neuroscience perspective on the process and its relation to psychopathology. *Psychological Medicine, 35,* 163–174.
Pasupathy, A., & Miller, E. K. (2005). Different time courses of learning-related activity in the prefrontal cortex and striatum. *Nature, 433,* 873–876.

Poldrack, R. A., Prabhakaran, V., Seger, C. A., & Gabrieli, J. D. (1999). Striatal activation during acquisition of a cognitive skill. *Neuropsychology, 13,* 564–574.
Pontieri, F. E., Tanda, G., Orzi, F., & Di Chiara, G. (1996). Effects of nicotine on the nucleus accumbens and similarity to those of addictive drugs. *Nature, 382,* 255–257.
Romeo, R. D., & Sisk, C. L. (2001). Pubertal and seasonal plasticity in the amygdala. *Brain Research, 889,* 71–77.
Rubia, K., Smith, A. B., Woolley, J., Nosarti, C., Heyman, I., Taylor, E., et al. (2006). Progressive increase of frontostriatal brain activation from childhood to adulthood during event-related tasks of cognitive control. *Human Brain Mapping, 27,* 973–993.
Schultz, W., Tremblay, L., & Hollerman, J. R. (2000). Reward processing in primate orbitofrontal cortex and basal ganglia. *Cerebral Cortex, 10,* 272–284.
Sisk, C. L., & Foster, D. L. (2004). The neural basis of puberty and adolescence. *Nature Neuroscience, 7,* 1040–1047.
Somerville, L. H., & Casey, B. J. (2010). Developmental neurobiology of cognitive control and motivational systems. *Current Opinion in Neurobiology, 20,* 1–6.
Spear, L. P. (2000). The adolescent brain and age-related behavioral manifestations. *Neuroscience and Biobehavioral Reviews, 24,* 417–463.
Spicer, J., Galvan, A., Hare, T. A., Voss, H., Glover, G., & Casey, B. (2007). Sensitivity of the nucleus accumbens to violations in expectation of reward. *Neuroimage, 34,* 455–461.
Steinberg, L. (2004). Risk taking in adolescence: What changes, and why? *Annals of the New York Academy of Sciences, 1021,* 51–58.
Steinberg, L. (2008). A social neuroscience perspective on adolescent risk-taking. *Developmental Review, 28,* 78–106.
Talairach, J., & Tournoux, P. (1988). *Co-planar stereotaxic atlas of the human brain* (M. Rayport, Trans.). New York: Thieme.
Thomas, K. M., Drevets, W. C., Whalen, P. J., Eccard, C. H., Dahl, R. E., Ryan, N. D., et al. (2001). Amygdala response to facial expressions in children and adults. *Biological Psychiatry, 49,* 309–316.
Tottenham, N., Tanaka, J., Leon, A. C., McCarry, T., Nurse, M., Hare, T. A., et al. (2009). The NimStim set of facial expressions: Judgments from untrained research participants. *Psychiatry Research, 168,* 242–249.
Vaidya, C. J., Austin, G., Kirkorian, G., Ridlehuber, H. W., Desmond, J. E., Glover, G. H., et al. (1998). Selective effects of methylphenidate in attention deficit hyperactivity disorder: A functional magnetic resonance study. *Proceedings of the National Academy of Sciences, U.S.A., 95,* 14494–14499.
Van Leijenhorst, L., Zanolie, K., Van Meel, C. S., Westenberg, P. M., Rombouts, S. A., & Crone, E. A. (2010). What motivates the adolescent? Brain regions mediating reward sensitivity across adolescence. *Cerebral Cortex, 20,* 61–69.
Velanova, K., Wheeler, M. E., & Luna, B. (2008). Maturational changes in anterior cingulate and frontoparietal recruitment support the development of error processing and inhibitory control. *Cerebral Cortex, 18,* 2505–2522.
Wise, R. A. (2004). Dopamine, learning and motivation. *Nature Reviews Neuroscience, 5,* 483–494.
Yurgelun-Todd, D. (2007). Emotional and cognitive changes during adolescence. *Current Opinion in Neurobiology, 17,* 251–257.